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Structure and Synthesis of Acid A, an Oxidation Product of Lycoramine

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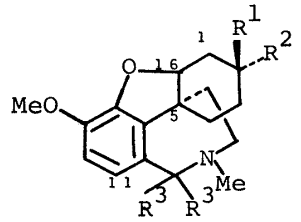
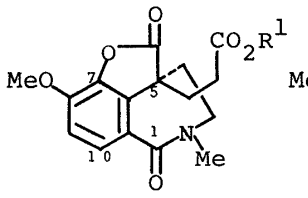
The structure of acid A, an oxidation product of lycoramine (**1**), an Amaryllidaceae alkaloid, was established as **4** on the basis of spectral and chemical evidence. The racemic methyl ester (**8**) of acid A (**4**) was synthesized.

Keywords——lycoramine; Amaryllidaceae; *Lycoris radiata*; oxolycoramine; oxolycoraminone; acid A; permanganate oxidation; acid A synthesis

During studies on the structure of the alkaloid lycoramine,[2a] present in *Lycoris radiata* HERB. (Amaryllidaceae), in 1938, Ishiwata[2b] isolated a carboxylic acid, $C_{17}H_{21}NO_6$,[2b] (named "acid A," mp 222—223 °C) by stepwise oxidation of the alkaloid, but did not elucidate its structure. After the structure of the alkaloid (**1**) had been determined,[3] the structure of acid A was proposed to be **4**, depicted in Chart 1.[4a] This paper deals with the stepwise oxidation of lycoramine (**1**) and with the structural elucidation of acid A (**4**) on the basis of spectral evidence and by synthesis of its racemic ester (**8**).



1: R^1=OH, R^2=R^3=H
2: R^1=OH, R^2=H, R^3,R^3=O
3: R^1,R^2=O, R^3,R^3=O



4: R^1=H
5: R^1=Me
6: R^1=Et

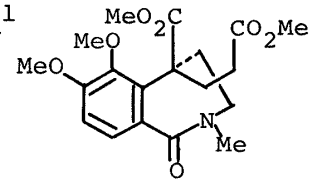


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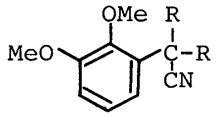
Chart 1

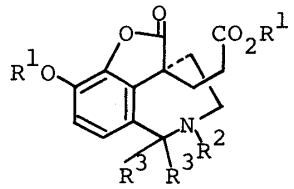
Oxidation of lycoramine (**1**) with 1% potassium permanganate at room temperature gave oxolycoramine (lycoramine lactam)[4b] (**2**) [mp 247—249 °C, $C_{17}H_{21}NO_4$; ν_{max} 3350 (OH) and 1620 (–NMe–C=O) cm^{-1}; δ_H 7.42 (d, 11-H) and 3.14 (NMe)]. Oxidation of **2** in pyridine with chromic oxide gave oxolycoraminone (lycoraminone lactam)[4b] (**3**): mp 216—218 °C, $C_{17}H_{19}NO_4$; ν_{max} 1710 (C=O) and 1640 (NMe–C=O) cm^{-1}; δ_H 7.40 (d, 11-H) and 3.16 (NMe). Oxidation of **3** in water with potassium permanganate at 3—4 °C gave acid A (**4**) [mp 218—221 °C, $C_{16}H_{17}NO_6$, $[\alpha]_D$ −48.9 °], which was found to be identical with an authentic sample of acid A (mp 222—223 °C, obtained by Ishiwata [2b]) by the mixed melting point test.

Spectroscopic examination of **4** revealed the presence of a γ-lactone (ν_{max} 1810 cm^{-1}), a carboxyethyl group [ν_{max} 1730 cm^{-1}; *m/z* 247 (base peak) $(M-CH_2=CH-CO_2H)^+$],[5] and an *N*-methyllactam [ν_{max} 1630 cm^{-1}; δ_H 3.10 (NMe) and 7.79 (10-H)]. These findings were supported by the following chemical evidence: esterification of **4** with diazomethane and with dry ethanol in the presence of sulfuric acid gave its methyl ester (**5**) [mp 112—113 °C, $C_{17}H_{19}NO_6$, $[\alpha]_D$ −73.5°; δ_H 3.55 (CO_2Me)] and ethyl ester (**6**) (mp 118—120 °C), respectively. Alkaline hydrolysis of the lactone ring in **4** and then methylation with diazomethane gave a dimethyl ester (**7**), mp 134—136 °C, $C_{19}H_{25}NO_7$; δ_H 3.59, 3.65, 3.74, and 3.87 (OMe × 4). From these results acid A was concluded to be **4**.



9: R=H

10: R=$CH_2CH_2CO_2Me$



8: R^1=R^2=Me, R^3,R^3=O

13: R^1=R^2=H, R^3,R^3=O

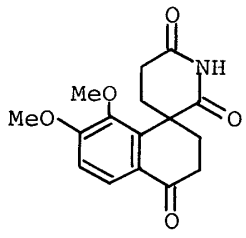
14: R^1=Me, R^2=H, R^3,R^3=O

15: R^1=Me, R^2=R^3=H

16: R^1=Me, R^2=H, R^3,R^3=S

17: R^1=R^2=Me, R^3=H

18: R^1=Me, R^2=CHO, R^3=H



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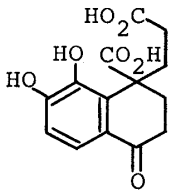

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Chart 2

This conclusion was confirmed by synthesis of the racemic methyl ester (**8**) of acid A as follows. Michael addition of 2,3-dimethoxybenzyl cyanide (**9**) in *tert*-butanol to methyl acrylate in the presence of Triton B gave a good yield of the γ-cyano ester (**10**) [ν_{max} 2250 and 1730 cm^{-1}], which was cyclized with polyphosphoric acid at 90 °C to give the spiro product (**11**) [ν_{max} 1710, 1695, and 1680 cm^{-1}] (32% yield). Hydrolysis of the imido ring of **11** with hydroiodic acid under reflux, accompanied by demethylation, gave the phenolic diacid (**12**) in good yield. Then, Schmidt reaction of the diacid (**12**) in phosphoric acid with sodium azide at 60 °C, accompanied by lactonization, gave (in 40% yield) only the lactam (**13**)[6] [ν_{max} 1820, 1740, and 1640 cm^{-1}; *m/z* 291 (M^+)], which was methylated with diazomethane to give the corresponding ester (**14**) quantitatively. An attempt to obtain the racemic ester (**8**) of acid A directly by methylation of the amide (**14**) with sodium hydride and methyl iodide, however, led to recovery of the starting material (**14**). The inability of **14** to undergo N-methylation is probably due to formation of an imide $-C(C=O)N^-\text{---}C^+(OMe)-O^-Na^+$, between the nitrogen atom and the carbonyl carbon atom of the ester group. Thus, we carried out N-methylation at the step of the secondary amine (**15**), as follows. Reduction of the lactam (**14**) to the amine (**15**) in 46% yield was achieved indirectly by treatment of **14** in toluene with phosphorus pentasulfide–potassium sulfide, and desulfuration of the resulting thiolactam (**16**) in dioxane with Raney-Ni under reflux. The amine (**15**) thus obtained was characterized as its picrate [mp 177—178 °C; ν_{max} 3150, 1805, and 1725 cm^{-1}]. Eschweiler–Clarke methylation of **15** gave a good yield of the tertiary amine (**17**), which was characterized as its hydrochloride [δ_H 2.86 (NMe)]. Oxidation of the amine (**17**) with 1% potassium permanganate in acetone in the presence of magnesium sulfate gave, along with formamide (**18**) [ν_{max} 1800, 1730, and 1670 cm^{-1}; δ_H 8.04 (1H, d, *J*=3 Hz, NCHO)], the desired racemic lactam (**8**), mp 117—

118 °C, which was found to be identical with the methyl ester (**5**) of acid A by comparison of their spectral data. Consequently, the stereochemistry of acid A was established as **4**, by taking into account the structure of lycoramine (**1**).

Experimental

All melting points are uncorrected. The spectrophotometers used were a JEOL model JNM-PS-100 or an FX-200 for nuclear magnetic resonance (NMR) spectra with tetramethylsilane (TMS) as an internal standard, a JEOL model JMS-D-300 for mass spectra (MS), and a Hitachi model 215 for infrared (IR) spectra. The plates used for preparative thin-layer chromatography (PTLC) were coated with silica gel (Kieselgel, PF_{254} Merck). Aluminum oxide 90 (activity II-III, Merck) and silica gel (Kieselgel 70—325 mesh, Merck) were used for column chromatography.

Oxolycoramine (2)——A 1% $KMnO_4$ solution (180 ml) was added to a solution of **1** (2 g) in H_2O (100 ml) under stirring at room temperature during 10 h. The reaction mixture was filtered to give a precipitate (a mixture of MnO_2 and the product), and the filtrate was concentrated under reduced pressure. The precipitate and residue were combined, digested in hot $CHCl_3$ (100 ml), and filtered. The filtrate was dried on Na_2SO_4 and evaporated to give a yellow powder (**2**) (1.3 g, 62.0%), which was recrystallized from EtOH as yellow prisms (0.9 g), mp 247—249 °C. $[\alpha]_D^{25}$ −94.8° (c=0.21, EtOH). *Anal.* Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.21; H, 6.79; N, 4.78. High MS m/z: Found: 303.1460. Calcd for $C_{17}H_{21}NO_4$: 303.1471. MS m/z (%): 303 (M^+, 78), 285 (63), 231 (58), 188 (100). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 1620 (N(Me)−C=O). ^{1}H-NMR ($CDCl_3$–pyridine-d_5) δ: 1.64 (1H, dd, J=16.0, 2.0 Hz, 1-βH), 1.91 (1H, dt, J=16.0, 4.0 Hz, 1-αH), 3.14 (3H, s, NMe), 3.18 (1H, ddd, J=13.0, 6.0, 3.0 Hz, 7-αH), 3.67 (1H, d-like, J=13.0 Hz, 7-βH), 3.88 (3H, s, OMe), 4.08 (1H, m, 2-H), 4.35 (1H, dd, J=4.0, 2.0 Hz, 16-H), 6.82 (1H, d, J=8.0 Hz, 12-H), 7.42 (1H, d, J=8.0 Hz, 11-H).

Oxolycoraminone (3)——A solution of **2** (1.33 g) in pyridine (40 ml) was added to a solution of CrO_3 (1.33 g) in pyridine (26 ml). The mixture was stirred at 50 °C for 8 h, then evaporated *in vacuo* and the residue was extracted with $CHCl_3$ (500 ml). The extract was washed successively with 10% H_2SO_4 and 5% Na_2CO_3, dried over Na_2SO_4, and evaporated to give a solid (**3**) (1.1 g, 83.3%), which was chromatographed on aluminum oxide with $CHCl_3$. The eluate with $CHCl_3$ gave **3** (0.9 g) as colorless prisms, mp 216—218 °C (from EtOH). $[\alpha]_D^{24}$ −239.1° (c=0.53, EtOH). *Anal.* Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.63; H, 6.19; N, 4.64. High MS m/z: Found: 301.1303. Calcd for $C_{17}H_{19}NO_4$: 301.1315. MS m/z (%): 301 (M^+, 100), 245 (28), 203 (24), 201 (26). IR ν_{max}^{KBr} cm^{-1}: 1715 (C=O), 1640 (N(Me)−C=O). ^{1}H-NMR ($CDCl_3$) δ: 2.08 (2H, m, 6-H_2), 2.88 (1H, dd, J=12.0, 3.0 Hz, 1-H), 3.16 (3H, s, NMe), 3.21 (1H, ddd, J=12.0, 3.5, 1.5 Hz, 7-αH), 3.70 (1H, ddd, J=12.0, 6.0, 2.0 Hz, 7-βH), 3.88 (3H, s, OMe), 4.93 (1H, t, J=3.0 Hz, 16-H), 6.87 (1H, d, J=8.0 Hz, 12-H), 7.40 (1H, d, J=8.0 Hz, 11-H).

Oxidation of Oxolycoraminone (3)——An aqueous solution of 1% $KMnO_4$ (43 ml) was added to a mixture of **3** (0.2 g) and Na_2CO_3 (0.2 g) in H_2O (100 ml) under stirring at 3—4 °C during 4 h. The reaction mixture was filtered, and the filtrate was washed with $CHCl_3$ (50 ml) and evaporated. The residue was acidified with 15% HCl, and extracted with $CHCl_3$ (300 ml). The extract was dried over Na_2SO_4 and evaporated to give a yellow oil (**4**) (50 mg, 23.6%), which was purified by acidic aluminum oxide column chromatography with benzene, $CHCl_3$, and acetone successively. The eluate with acetone was evaporated to dryness, and the residue (**4**, acid A) was crystallized from EtOH as colorless prisms. mp 218—221 °C. $[\alpha]_D^{23}$ −48.9° (c=0.80, EtOH). *Anal.* Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 60.34; H, 5.43; N, 4.48. High MS m/z: Found: 319.1033, 247.0837. Calcd for $C_{16}H_{17}NO_6$ (M^+): 319.1056, $C_{13}H_{13}NO_4$: 247.0843. MS m/z (%): 319 (M^+, 88), 247 (100), 232 (50), 203 (60). IR ν_{max}^{KBr} cm^{-1}: 1810 (γ-lactone), 1730 (COOH), 1630 (N(Me)−C=O). UV λ_{max}^{EtOH} nm (log ε): 253 (4.08), 285 (3.54). ^{1}H-NMR (pyridine-d_5) δ: 3.10 (3H, s, NMe), 3.80 (3H, s, OMe), 7.04 (1H, d, J=8.0 Hz, 9-H), 7.79 (1H, d, J=8.0 Hz, 10-H). The aqueous acidic solution separated above from the $CHCl_3$ layer was evaporated to dryness *in vacuo*. The residue was extracted with hot acetone, and the acetone solution was concentrated to give a yellow oil (130 mg), which was purified by acidic aluminum oxide column chromatography with benzene, $CHCl_3$, and acetone successively. The eluate with acetone gave colorless prisms of acid B (named by Ishiwata[2b]), mp 265—267 °C (dec.) (from methyl ethyl ketone). *Anal.* Calcd for $C_{17}H_{19}NO_6 \cdot H_2O$: C, 55.58; H, 5.76; N, 3.81. Found: C, 55.28; H, 5.72; N, 4.10. Its dimethyl ester, mp 165—167 °C (from benzene), $C_{19}H_{23}NO_7$, obtained by methylation of acid B in MeOH with ethereal diazomethane, was found to be identical with the methyl ester of acid B by direct comparison.

Acid A Methyl Ester (5)——A solution of diazomethane in ether was added to a solution of acid A (**4**) (4.5 mg) in dry MeOH (1 ml) and the mixture was allowed to stand overnight at 0 °C. Work-up in the usual way gave the methyl ester (**5**) (3.0 mg) of acid A as colorless needles, mp 112—113 °C, (from *n*-hexane–$CHCl_3$). $[\alpha]_D^{21}$ −73.5° (c=0.95, EtOH). High MS m/z: Found: 333.1199, 247.0834. Calcd for $C_{17}H_{19}NO_6$ (M^+): 333.1212, $C_{13}H_{13}NO_4$: 247.0843. MS m/z (%): 333 (M^+, 100), 260 (56), 247 (93), 232 (62), 203 (77). IR ν_{max}^{KBr} cm^{-1}: 1800 (γ-lactone), 1720 (COOMe), 1650 (N(Me)−C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.80—2.60 (6H, m, 4-H_2, 13-H_2, 14-H_2), 3.14 (3H, s, NMe), 3.14—3.55 (2H, m, 3-H), 3.55 (3H, s, COOMe), 3.97 (3H, s, OMe), 7.00 (1H, d, J=8.0 Hz, 9-H), 7.60 (1H, d, J=8.0 Hz, 10-H).

Acid A Ethyl Ester (6)——A mixture of **4** (17.4 mg) and conc. H_2SO_4 (1 drop) in EtOH (3 ml) was refluxed for

3 h, and evaporated *in vacuo*. Work-up in the usual way gave a solid (11 mg), which was recrystallized from EtOH, to give **6**, mp 118—120 °C. $[\alpha]_D^{20}$ −56.19° (*c* = 0.69, EtOH). High MS *m/z*: Found: 347.1353. Calcd for $C_{18}H_{21}NO_6$ (M^+): 347.1369. IR ν_{max}^{KBr} cm^{-1}: 1810 (γ-lactone) 1720 (COOEt), 1645 (N(Me)−C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.19 (3H, t, *J* = 7.0 Hz, $CH_2C\underline{H}_3$), 1.64—2.68 (6H, m, 4-H_2, 13-H_2, 14-H_2), 3.16 (3H, s, NMe), 3.20—3.70 (2H, m, 3-H_2), 3.98 (3H, s, OMe), 4.00 (2H, q, *J* = 7.0 Hz, $C\underline{H}_2CH_3$), 7.01 (1H, d, *J* = 8.0 Hz, 10-H), 7.60 (1H, d, *J* = 8.0 Hz, 9-H).

Hydrolysis of the Lactone Ring of Acid A (4), Followed by Methylation——A solution of **4** (40 mg) in 17% KOH–EtOH (23 ml) was refluxed for 5 h, and evaporated *in vacuo*. Me_2SO_4 (16 ml) and 10% KOH (45 ml) were added dropwise to a solution of the residue in H_2O (15 ml) with stirring, and stirring at 20—25 °C was continued for 3 d. The reaction mixture was acidified with H_2SO_4, and extracted with $CHCl_3$ (1.3 l). Evaporation of the $CHCl_3$ extract gave a yellow oil (40 mg), which was methylated with diazomethane to give **7** as colorless needles, mp 134—136 °C (from benzene). High MS *m/z*: Found: 379.1630. Calcd for $C_{19}H_{25}NO_7$ (M^+): 379.1631. ^{1}H-NMR ($CDCl_3$) δ: 1.80—2.60 (6H, m, 4-H_2, 13-H_2, 14-H_2), 3.05 (3H, s, NMe), 3.00—3.50 (2H, m, 3-H_2), 3.59 (3H, s, 14-COOMe), 3.65 (3H, s, 5-COOMe), 3.74 (3H, s, 8-OMe), 3.87 (3H, s, 7-OMe), 6.91 (1H, d, *J* = 8.0 Hz, 9-H), 7.52 (1H, d, *J* = 8.0 Hz, 10-H).

Michael Addition of Methyl Acrylate with 2,3-Dimethoxybenzyl Cyanide (9)——A mixture of 40% methanolic Triton B (20 ml) and *tert*-butanol (28 ml) was added dropwise to a solution of the 2,3-dimethoxybenzyl cyanide (**9**) (23 g) and methyl acrylate (55 ml) in *tert*-butanol (60 ml) under reflux. The mixture was heated under reflux for 6 h, and concentrated under reduced pressure to give a residue, which was taken up in $CHCl_3$. The $CHCl_3$ solution was washed with aqueous $NaHCO_3$ and water, dried over Na_2SO_4 and concentrated. The residue was subjected to fractional distillation to give the pimelate (**10**) (32 g, 70.6%), bp 180—185 °C/0.2 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250 (CN), 1730 (C=O).

Treatment of the Pimelate (10) with Polyphosphoric Acid——A mixture of the pimelate (**10**) (7 g) and polyphosphoric acid (210 g) was heated at 90 °C for 6 h, diluted with water, and concentrated to give the imide (**11**) (1.95 g, 32.1%), mp 290—291 °C (from $CHCl_3$–ether). *Anal.* Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.13; H, 5.45; N, 4.53. IR ν_{max}^{KBr} cm^{-1}: 1710, 1695, 1680 (C=O).

Hydrolysis of the Imide (11) with Hydroiodic Acid——A solution of the imide (**11**) (5.55 g) in hydroiodic acid (80 ml) (constant-boiling acid (bp 127 °C)) was heated under reflux for 30 min, and poured into ice water. The aqueous solution was made slightly acidic by adding Na_2CO_3 and extracted with AcOEt. The extract was washed with aqueous $Na_2S_2O_3$ and brine, dried, and concentrated to give a keto-phenolic acid (**12**) (4.1 g, 76.1%), mp 178—180 °C (orange-yellow needles) which was, without further purification, subjected to Schmidt reaction, since the keto-phenolic acid (**12**) was not stable enough to be stored.

Schmidt Reaction of the Keto-phenolic Acid (12)——Sodium azide (500 mg) was added in several portions to a solution of the keto-acid (**12**) (1.14 g) in 85% H_3PO_4 at 60 °C for 6 h. The mixture was diluted with water, made slightly acidic by adding Na_2CO_3, and extracted with AcOEt. The extract was washed with a small amount of brine, dried and concentrated to give the lactam (**13**) (456 mg, 40.4%), mp 260—261 °C (from MeOH–AcOEt). *Anal.* Calcd for $C_{14}H_{13}NO_6$: C, 57.73; H, 4.50; N, 4.82. Found: C, 57.45; H, 4.80; N, 4.89. IR ν_{max}^{KBr} cm^{-1}: 1820 (γ-lactone), 1740 (COOH), 1640 (NH−C=O).

Methylation of the Lactam (13)——The lactam (**13**) (440 mg) was treated with ethereal diazomethane in MeOH–tetrahydrofuran (THF) in the usual way to give the ester (**14**) (435 mg, 90.2%), mp 180—181 °C, as needles (from MeOH). *Anal.* Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 60.31; H, 5.59; N, 4.43. IR ν_{max}^{KBr} cm^{-1}: 1820 (γ-lactone), 1740 (COOMe), 1665 (NH−C=O).

The Thiolactam (16)——A suspension of the lactam (**14**) (40 mg), phosphorus pentasulfide (200 mg), and potassium sulfide (300 mg) in toluene (30 ml) was stirred at 80 °C for 1.5 h and filtered. The precipitate was thoroughly washed with toluene. The washings were combined with the filtrate, and the whole was concentrated under reduced pressure to give a residue, which was chromatographed on silica gel in CH_2Cl_2. The eluate gave the thiolactam (**16**) (400 mg, 82.8%), mp 139—140 °C (from MeOH–*n*-hexane). *Anal.* Calcd for $C_{16}H_{17}NO_5S$: C, 57.30; H, 5.11; N, 4.18; S, 9.50. Found: C, 57.04; H, 5.40; N, 4.40; S, 9.27. IR ν_{max}^{KBr} cm^{-1}: 3150 (NH), 1800 (γ-lactone), 1730 (COOMe).

Reduction of the Thiolactam (16) with Raney Ni——A suspension of the thiolactam (**16**) (100 mg) and Raney Ni (prepared from 3 g of Raney alloy) in 80% aqueous dioxane (10 ml) was heated under reflux for 1.5 h and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was washed with ether. The ethereal washings were treated with an ethereal solution of picric acid to precipitate the picrate (90 mg) of the amine (**15**), mp 177—178 °C (from MeOH). *Anal.* Calcd for $C_{16}H_{19}NO_5 \cdot C_6H_3N_3O_7$: C, 49.44; H, 4.15; N, 10.48. Found: C, 49.73; H, 4.39; N, 10.40. IR ν_{max}^{KBr} cm^{-1}: 3150 (N^+H_2), 1805 (γ-lactone), 1725 (COOMe).

N-Methylation of the Amine (15)——A mixture of the amine (**15**) (80 mg), 37% formalin (2.5 ml) and formic acid (2.5 ml) was heated under reflux for 4 h and concentrated under reduced pressure to give a residue, which was treated with a few drops of 6 N hydrochloric acid. The mixture was concentrated to give the *N*-methylamine (**17**) hydrochloride (65 mg, 69.7%), mp 226—228 °C (from EtOH). *Anal.* Calcd for $C_{17}H_{21}NO_5 \cdot HCl$: C, 57.38; H, 6.23; N, 3.94; Cl, 9.96. Found: C, 57.18; H, 6.48; N, 4.09; Cl, 9.97. IR ν_{max}^{KBr} cm^{-1}: 1800 (γ-lactone), 1725 (COOMe). ^{1}H-NMR ($CDCl_3$) δ: 7.17, 7.09 (1H each, AB-q, *J* = 8.5 Hz, 11-H, 12-H), 3.95, 3.45 (3H each, s, OMe), 2.86 (3H, s, NMe).

Oxidation of the *N*-Methylamine (17) ((±)-Acid A Methyl Ester)——A solution of 1% potassium permanganate in acetone was added dropwise to a suspension of the amine hydrochloride (**17**–HCl) (260 mg) and anhydrous

Mg_2SO_4 (1 g) in acetone (60 ml) with stirring at room temperature. When the color of $KMnO_4$ was maintained in the reaction mixture, addition of $KMnO_4$ was stopped. The mixture was stirred for 1 h, bubbled with SO_2 gas, diluted with H_2O, and extracted with AcOEt. The extract was washed with H_2O, dried, and concentrated to leave a residue, which was subjected to PLC on silica gel with AcOEt–EtOH (7 : 1) to give the (±)-acid A methyl ester (**5**) (3 mg), which was shown to be identical with an authentic sample of acid A methyl ester derived from lycoramine (**1**) by IR ($CHCl_3$), ultraviolet (UV), and MS comparisons, together with an *N*-formyl ester (**18**) (7 mg), mp 124—125 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1800, 1730, 1670 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.55, 3.93 (3H each, s, OMe), 4.40, 5.12 (1H each, AB-q, J=14 Hz, $PhCH_2N$), 6.82, 7.08 (1H each, AB-q, J=8.5 Hz, 11-H, 12-H), 8.04 (1H, s, NCHO).

References and Notes

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2) *a)* H. Kondo and S. Ishiwata, *Chem. Ber.*, **70**, 2427 (1937); *idem, Yakugaku Zasshi*, **58**, 1 (1938); *b)* S. Ishiwata, *ibid.*, **58**, 13 (1938). The formula ($C_{17}H_{21}NO_6$) of acid A was revised to $C_{16}H_{17}NO_6$ by us.
3) S. Kobayashi, T. Shingu, and S. Uyeo, *Chem. Ind.* (London), **1956**, 177; D. H. R. Barton and G. W. Kirby, *Proc. Chem. Soc., London*, **1960**, 329; *idem, J. Chem. Soc.*, **1962**, 806.
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5) This fragment ($C_{13}H_{13}NO_4$) at *m/z* 247 in the mass spectra of **4** and **5** (see Experimental) can be accounted for by McLafferty rearrangement of γ-H to the carbonyl oxygen atom of the lactone.
6) According to the previous paper [S. Uyeo, H. Irie, A. Yoshitake, and A. Ito, *Chem. Pharm. Bull.*, **13**, 427 (1965)], the fact that Schmidt reaction of **12** gave only the product (**13**) can be accounted for by the effect of a hydroxyl group *para* to the carbonyl group in **12**.
7) The structure of acid B will be reported elsewhere.